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*The Bradshaw Lecture*

*Sir Frederic Eve, F.R.C.S.*



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# ACUTE HAEMORRHAGIC PANCREATITIS:

WITH REMARKS ON THE ETIOLOGY OF  
CHRONIC PANCREATITIS.

## *The Bradshaw Lecture*

DELIVERED BEFORE THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

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ON  
ACUTE HAEMORRHAGIC PANCREATITIS ;  
WITH REMARKS ON THE ETIOLOGY OF  
CHRONIC PANCREATITIS.

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MR. PRESIDENT AND GENTLEMEN,—Ten years have passed since Mayo Robson, who had made this subject his own, discoursed in this theatre on pancreatitis. During that period so much light has been thrown on the subject by the experimental pathologist and the clinician that no excuse is required for reopening it.

ACUTE PANCREATITIS.

The macroscopic changes of acute haemorrhagic pancreatitis are extremely characteristic and find no counterpart in any other organ.

*Macroscopic Appearances.*

In the earlier stages the pancreas is swollen, friable, and mottled red or brown to black with haemorrhages, which lie chiefly near the surface or in the interstitial connective tissue. Areas of opaque white or yellow fat necrosis are observed in the peripancreatic fat and in that of the septa. They are also commonly met with in the fat of the omentum and mesentery. In some cases their distribution is very wide, and fat necrosis may be seen in the subperitoneal fat of the abdominal wall, retroperitoneal adipose tissue, and even in the subpericardial and subpleural fat. A sanguineous or sero-sanguineous effusion is encountered in the lesser cavity of the peritoneum. This fluid is at first often sterile and contains products of pancreatic secretion, but it soon becomes infected; and in cases of some duration, or even



at an early stage in some very acute cases, septic peritonitis exists.

If the patient survives, varying degrees of necrotic and of suppurative changes are observed in and around the pancreas. Cases have been recorded in which the pancreas was necrosed and sequestered in its entirety. This may have occurred, but Dr. Turnbull informs me that the sequestered necrotic masses he has met with were composed of blocks of peripancreatic adipose tissue, and not of the pancreas itself. In two cases the house-surgeon assured him that the whole pancreas had sloughed through a laparotomy wound; but in both instances the pancreas was found in its normal position at the necropsy.

Suppuration of a diffuse character occurs mainly in the tissue around the pancreas; at times, in less acute cases, a localized abscess forms in the pancreas itself.

The original subdivision by Fitz of acute pancreatitis into haemorrhagic, gangrenous, and suppurative, merely represents the outstanding pathological features of different cases exhibiting varying stages and degrees of the malady. The haemorrhages are always associated with necroses, although one may be more conspicuous than the other; and they are both the primary result of the same morbid process. This, of course, does not imply that a primary haemorrhage into the pancreas from changes in the blood or blood vessels never occurs; but such an apoplexy would be distinct from acute haemorrhagic pancreatitis.

### *Histology.*

The specimens I have studied confirm the description of the histological appearances given by Opie.<sup>1</sup> The chief features are: Areas of necrosis involving the parenchyma and also the interlobular septa; haemorrhages most abundant about the periphery of the gland and around the necrotic areas; in addition, a diffuse infiltration of the septa, and, to a less extent, the gland substance with red corpuscles; there are also patches of fat necrosis involving the periglandular fat and the adipose tissue in the septa (see Plate, Figs. 1 to 4).

Of six specimens in the Pathological Institute of the London Hospital all but one showed definite evidence of



inflammation, such as masses of polymorphonuclear leucocytes and areas of purulent infiltration around patches of necrosis (see Plate, Fig. 2), in the septa, and beneath the peritoneum. The veins in some instances contained red or mixed thrombi, and occasionally the arteries were thrombosed.

In one case only (see Plate, Fig. 1) out of six the leucocytic infiltration was very restricted, and limited to a few areas around necroses, although the patient died on the sixth day, while in all the others death occurred on or before the fourth day. Opie, among five specimens examined microscopically, observed one in which there was little or no inflammatory reaction.<sup>2</sup>

Some writers regard all the changes in acute pancreatitis as the result of the action of the pancreatic secretion on the gland. Chiari<sup>3</sup> describes it as a tryptic auto-digestion; others (Fitz, Körte) regard the disease as an acute haemorrhagic inflammation leading to necrosis. Guleke recognizes two forms of the disease—a necrotic form, which he calls “pancreatic necrosis”; and an inflammatory form, provoked by bacterial inflammation, which he names “acute pancreatitis.” He considers that the two forms are not sharply defined.

I propose to show that both the digestive and the inflammatory hypotheses are in part true, in that the process in the initial stage is due to aseptic or bacterial infection, which not only lowers the resistance of and damages the gland tissue, but also liberates trypsin. The action of this proteolytic ferment, together with that of the steapsin, give to the morbid process its characteristic changes.

The pancreatic juice presents this peculiarity, that when secreted its principal digestive agent is inert. The trypsin or proteolytic enzyme is secreted as an inactive substance—trypsinogen—and this is activated or transformed into trypsin by enterokinase, a substance said to be an enzyme, which is produced by the intestinal mucous membrane. The activation of the pancreatic secretion takes place after it is poured into the intestine, and therefore under normal circumstances the pancreas runs no danger of self-digestion.

According to Professor Starling, the juice obtained from the pancreatic duct by the use of secretin contains only trypsinogen. And Dr. H. M. Vernon, whose work on the pancreatic secretion is well known, writes to me that "probably under ordinary circumstances enterokinase is the only agent that can start the activation of trypsinogen; but both juice and extracts contain also another ferment in zymogen-form, which, when set free, is much more powerful than enterokinase. So long as this ferment is present as zymogen the juice will remain inactive, whether in the ducts or elsewhere, and it is only when it is rendered active by the slow action of free trypsin that it is able to exert its rapid activating influence on trypsinogen."

This new fact, just discovered by Dr. Vernon, would appear at first sight to have no bearing on the etiology of acute pancreatitis, for the trypsin is, under normal conditions, developed outside the pancreas by the action of the enterokinase of the succus entericus.

It must be taken in conjunction with an observation by Mellanby and Woolley,<sup>4</sup> that *Bacillus coli* and other intestinal flora are capable of activating pancreatic juice. These bacteria, according to Dr. Vernon, secrete powerful proteolytic ferments similar to trypsin, and he holds that the ferments secreted by them liberate an activator from the zymogen above referred to, and that it is this, and not enterokinase, which produces the effect observed.

To put the matter shortly, there is, on physiological grounds, good reason for believing that bacteria, and especially the *B. coli*, are capable of activating the pancreatic secretion independently of enterokinase. This, as we shall subsequently see, is entirely in accord with the results obtained by experiments on the artificial production of acute pancreatitis.

In addition to an amylolytic enzyme, the pancreatic juice also contains a fat-splitting enzyme, steapsin, capable of splitting neutral fats into fatty acids and glycerine, and it is this ferment which causes the fat necrosis. Bile increases the activity of steapsin two-fold (Neucke and Bremo). This is corroborated by Mellanby and Woolley,



and, as we shall see, is another fact having an important pathological bearing.

### *Experimental Pathology.*

Opie was the first to show that there was a definite relation between cholelithiasis and acute pancreatitis. In an autopsy on a case of Halsted's he found a gall stone impacted in and filling the diverticulum. In a subsequent

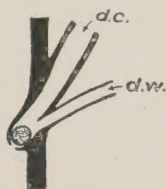


Fig. I. — Diagram, after Opie, to show a calculus blocking the papilla, and permitting of a free channel between the ductus choledochus and the duct of Wirsung.

case a small stone blocked the orifice of the diverticulum but did not fill it, so that a direct channel was formed between the biliary and the pancreatic ducts (Fig. I). That bile had flowed into the pancreatic duct was demonstrated by the duct being stained bright green. Acting on this hint he injected bile into the pancreatic duct of dogs, and found that the injection of 5 c.cm. caused death

with haemorrhagic inflammation and fat necrosis. This at first sight conclusive fact was only the starting point of a long series of experiments. So many have been made with various substances that time will only permit allusion to a few of them.

At the outset it may be remarked that many of these experiments, although resulting in a condition resembling acute haemorrhagic pancreatitis, do not reproduce the conditions existing during life. The pressure of the secretion of the bile and pancreatic juice is very low, even supposing, as Flexner suggests, that the bile pressure is accentuated by contraction of the gall bladder; whereas in experiments the injection is made with a syringe, and considerable amounts, 5 or 10 c.cm., were often used. That the amount injected has a relation to the result was shown by Opie and many others with bile. Death did not follow the use of smaller amounts than 5 c.cm., and the changes produced in the organ were less widespread and severe. The pancreas is a very loose gland, the walls of the terminal ducts extremely thin, so that fluids under slight pressure would readily be extravasated into the gland tissue.

Many of the substances employed in experiments—zinc chloride, nitric and chromic acid—would act as irritants to the walls of the blood vessels and gland cells, and produce haemorrhages and necrosis. Flexner showed that the action of bile, which will dissolve red blood corpuscles, is due to the cytolytic property of the biliary salts. Olive oil, injected with positive results by Hess and others, owes its action to the liberation of fatty acids, which are extremely irritating to the tissues.

Other substances employed are not only irritants, but may also activate the pancreatic juice; for example, solutions of hydrochloric acid to imitate gastric juice. Dr. Vernon informs me that if pancreatic juice be partly neutralized by hydrochloric acid it spontaneously activates itself. Mellanby and Woolley also state that removal of the alkali of pancreatic juice by neutralization with hydrochloric acid produces rapid activation. To the same category belong solutions of various species of bacteria injected by a number of experimenters. Inert substances, such as blood, blood serum, glycerine, paraffin, agar-agar, gave a negative result.

Starling failed to induce any change in the gland by injecting enterokinase into its duct. He used succus entericus freed from micro-organisms by filtering through porcelain. Ligature of the duct of Wirsung causes no change beyond fibrosis, probably a fibrotic atrophy. By an exhaustive series of experiments on dogs, Polya<sup>5</sup> conclusively proved that the pathological picture of acute haemorrhagic pancreatitis can be reproduced by injecting solutions of active pancreatic extract and pancreatic juice.

Among 33 dogs injected, 19 died within twenty-four hours and 4 others within six days. In most of these animals punctiform haemorrhages appeared on the surface of the pancreas immediately after the injection; these quickly extended over the greater part of the gland. The animals died in an apathetic condition with laboured and rapid respiration, and cramps were often observed. Autopsies showed effusion of blood-stained serum into the peritoneal cavity and widespread fat necrosis. The pancreas was greatly swollen and more or less infiltrated with blood. Microscopically there were varying degrees of parenchymatous digestion up to complete necrosis, in addition to haemorrhages.

Trypsin completely destroyed by heat gave negative results. The intensity of the lesions depended on the proteolytic



activity of the trypsin, not on the quantity of solution injected; 2 or 3 c.cm., or even 1 c.cm., of an active solution caused death. The action of trypsin is a local one, producing oedema, haemorrhages, and necrosis.

Other experimenters found that the same changes ensue on injecting solutions containing trypsin into various structures, as peritoneum, skin, subcutaneous tissue, and the tongue of frogs.

Polya also injected intestinal contents, cultures of bacteria, and bile infected with bacteria. He arrived at the following conclusions:

Typical pancreatic necrosis with haemorrhages, fat necrosis and a rapidly fatal course, may be originated most certainly with strongly active trypsin solution, less constantly by duodenal contents and by bile mixed with bacteria, rarely by the contents of intestinal fistulae and extract of intestinal mucous membrane, and only exceptionally by bacteria alone. His experiments with infected bile showed that in *small* quantity it gave rise to as extensive changes (that is, pancreatitis and fat necrosis) as a *large* quantity of normal bile.

After the injection of cultures of bacteria or filtrates of cultures, suppurative interstitial inflammations without necrosis were for the most part observed, and in one-third of the cases the pancreas remained normal.

The inconclusive results obtained by the injections of bacteria probably, as Nordmann suggests, were due to the fact that he did not occlude the orifices of both pancreatic ducts before making the injection (see Fig. II). Nevertheless, Polya concluded that bacteria are capable of activating the pancreatic secretion and that their activating power is increased by bile. With regard to the latter point, Professor Starling assures me that bile is not an activator; and it may be noted that Polya does not mention having tested the activating power of bacteria experimentally with juice from pancreatic fistulae.

Polya's experiments, however, demonstrate in a striking manner the master rôle played by auto-digestion in the production of acute haemorrhagic pancreatitis, although the changes induced by the injection of trypsin differed from the majority of cases of acute pancreatitis in man, in that no leucocytic infiltration was observed.

As regards the possibility of duodenal secretion causing acute pancreatitis the evidence is all against the assumption that it regurgitates, except in very rare instances, into the pancreatic ducts. The papilla is provided with a

sphincter. Hess failed to produce pancreatitis by putting a cannula in the papilla unless the duodenum was actually occluded on the distal side. And the device of inserting a silk thread from the duodenum through the papilla into the pancreatic duct also failed.

Nordmann<sup>6</sup> instituted some further experiments with the object of explaining the relation between cholelithiasis and acute pancreatitis. He demonstrated that two factors are necessary for the production of acute haemorrhagic pancreatitis: (1) There must be complete stasis of the pancreatic juice within the ducts. (2) Bacteria with or without admixture of bile, must gain access to the stagnant secretion and multiply in it.

To understand these experiments it must be explained that in dogs the pancreas has two ducts which anastomose freely in the gland (Fig. II). The upper and smaller duct opens with the common bile duct into the ampulla as in man. The chief duct opens on the duodenum 3 to 5 cm. lower down. In order to produce any

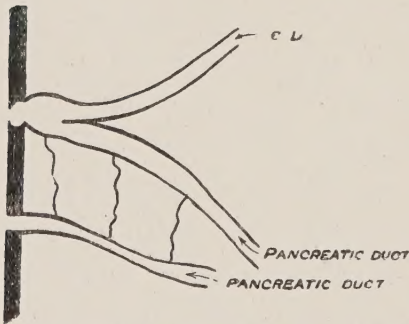


Fig. II.—Diagram (after Nordmann) to show the arrangement of the pancreatic ducts in a dog. C.D. Ductus choledochus.

change as the result of injecting bacteria, it was necessary that both ducts should be occluded. If the lower duct were left open the result was negative. Nordmann closed both ducts by running a suture of silkworm gut around their orifices. Bile was thus allowed to regurgitate from the ampulla into the pancreatic duct, yet

no morbid change resulted although the pancreatic secretion and the pancreatic duct were both stained with bile. But when, after closure of the pancreatic ducts, bacteria were injected into the gall bladder, typical haemorrhagic pancreatitis was produced.

The ampulla of dogs is often so small that a suture which closes the papilla also occludes the ampulla and shuts off the communication between the bile and pancreatic ducts. Nevertheless, even when this occurred the introduction of bacteria into the gall bladder was followed



by positive results. Evidently bacteria were able to wander through the intrapancreatic portion of the bile duct into the duct of Wirsung. Nordmann in his experiments injected into the gall bladder 0.5 c.cm. of a twenty-four hours' broth culture of mixed bacteria from the faeces of a dog. In other cases streptococci, staphylococci, or *Bacillus coli* from man were used, but the results were not so generally positive.

The animals died in forty-eight to sixty-five hours, and the clinical course of the malady, together with the macroscopic and microscopic changes, corresponded with those of acute haemorrhagic pancreatitis. In nearly half the cases there was a yellow colouring of the pancreatic duct. Collections of leucocytes were observed at the margins of the necrotic patches, but never in the middle of them. This corresponds with the description given above of the histological changes in acute pancreatitis in man. Wherever a haemorrhage was found he always observed near it a necrosis. Nordmann can find no reason for believing that there is ever primarily a digestion of intact tissue, as he never observed pure aseptic necrotic patches in the gland tissue. He "believes that an alteration of the tissue of the gland, possibly of a chemical nature, resulted through the dammed up pancreatic secretion, containing bacteria and sometimes mixed with bile, and that the typical necrosis takes place on the basis of these antecedent local tissue damages, which are found especially in the interstitial tissue, but also in the glandular lobules." He further thinks that "these tissue disturbances can possibly be produced by very different causes—namely, by injuries, by haemorrhages in consequence of angioneurotic disturbances, ischaemia, etc." This conclusion, although necessarily vague, as he does not take into account the activating properties of bacteria, is very near the mark.

To sum up, the experiments and facts brought forward warrant the assertion that acute haemorrhagic pancreatitis is, in the majority of cases, due to a bacterial infection. The bacteria appear to have a double action; they lower the resistance of the tissues by their toxins and by their proteolytic ferments activate the pancreatic

juice, which in its turn digests the damaged tissues. Obviously the process is largely due to the action of the pancreatic juice, or it would not be so constantly associated with fat necrosis. It must also be remembered that in certain cases in which diffusion of pancreatic secretion takes place without activation, fat necrosis only ensues. This is seen conspicuously in certain cases of injury.

The infective organism is most commonly a bacillus of the colon group. This, according to Egdahl,<sup>7</sup> is usually found in acute pancreatitis. It is also that most frequently isolated from bile in infective conditions of the biliary passages. It may be noted that colon bacilli were found in the pancreas and blood of one of Mayo Robson's<sup>21</sup> cases, in which an autopsy was performed three hours after an operation for acute pancreatitis. A specimen of acute pancreatitis, due to obstruction by a round worm of the papilla and the ducts of Wirsung and Santorini, showed very large numbers of *Bacillus coli* in the necrotic parts, especially in the septa, and enormous numbers under the peritoneal surface. Purulent infiltration was in this case well-marked. Dr. Twort, to whom the sections were shown, agreed that the bacilli were of the colon group. It would be difficult to devise experimentally conditions more favourable than those existing in this case for the production of acute pancreatitis, or which more completely fulfil Nordmann's premisses.

It has often been assumed that the haemorrhages are due to digestion of the walls of the blood vessels. The researches of Rickes, Natus, and Knappe, conducted on rabbits, show that they are the result of stasis in the blood vessels, and are of the nature of diapedesis haemorrhages. Trypsin produces similar effects on the blood vessel walls, as does a solution of salt of the same concentration as the pancreatic juice.

The infective theory of the origin of acute pancreatitis explains peculiarities pointed out to me by Turnbull. In many necropsies in which there was no evidence of pancreatitis the terminal portion of the duct of Wirsung has been noticed to be stained by bile. Further, cancerous obstruction of the papilla of Vater may lead to extreme



dilatation of the common bile duct and duct of Wirsung without causing fat necrosis; therefore, neither obstruction to the pancreatic ducts nor entrance of bile into the pancreatic ducts do by themselves produce acute pancreatitis.

*Lymphatic Origin of Pancreatitis.*

It has been shown that a free communication exists between the lymphatics of the pancreas and those of the gall bladder by means of the glands about the head of the pancreas, and Deaver<sup>8</sup> has observed in pancreatitis striking evidence of inflammatory changes in these glands. Both he and Arnsperger have therefore developed the idea that infection may be conveyed from the gall bladder to the pancreas by the lymphatics without any mechanical obstruction at the papilla. This appears to be excluded by an experiment of Nordmann. After closure of the pancreatic ducts, he ligatured the common bile duct distal to the gall bladder and then injected bacteria into it. A cholangitis followed but no pancreatitis.

*Etiology.*

Let us now consider how the facts obtained in the laboratory fit in with those observed in disease.

Clinical experience bears out the conclusions that stasis and infection are the main elements in the causation of acute pancreatitis, and these are most commonly brought about by cholelithiasis. Egdahl, in an analysis of 105 cases, found that in 44 (42 per cent.) the disease followed gall stones or suspected gall stones. But in only three of these cases was the stone in or near the ampulla. In 44 cases of Körte cholelithiasis existed in 21 (47 per cent.), and in 16 consecutive cases analysed by Dietrich<sup>9</sup> cholelithiasis was found at the operation or autopsy in 8. Calculi occupied the common bile duct only twice, and in both of these they were small and not impacted. Dietrich states that in his cases gall stones were certainly excluded only three times (18.75 per cent.).

At the London Hospital during the five years 1907-12 there were eleven autopsies on cases of acute haemorrhagic pancreatitis. Gall stones were present seven times (63.6 per cent.), and a round worm (in a case of Mr. Rigby) occluded both pancreatic ducts in an eighth. In

only one of these cases did the stone occupy the ampulla. In the remaining 6 cases the calculi were in the gall bladder and were invariably multiple and small. In 2 cases there was a duodenal ulcer, and in one of these a constriction of the common bile duct with dilatation of the pancreatic duct was noticed; therefore gall stones or obstruction at the papilla existed in nearly 82 per cent. of the cases. The duct of Wirsung showed evidence of stasis of secretion, or of infection in 7 cases out of the 11. It may be observed that a true estimate of the causes at work is more likely to be obtained from autopsies than from operations performed under conditions of grave illness, when the condition of the patient may preclude a careful examination of the bile passages.

The exact mechanism by which the pancreas is infected evidently varies. The figures quoted above show that the direct regurgitation of infected bile into the duct of Wirsung, owing to the impaction of a small calculus in the ampulla, occurs only in a small proportion of cases—about 20 per cent. The requisite anatomical conditions are shown in Fig. I, and exist only in 20 per cent. of subjects. According to the measurements by Opie of the diverticulum and of the orifice of the papilla, a stone sufficiently large to become impacted in the papilla would in 70 per cent. of cases also completely fill the diverticulum, so that

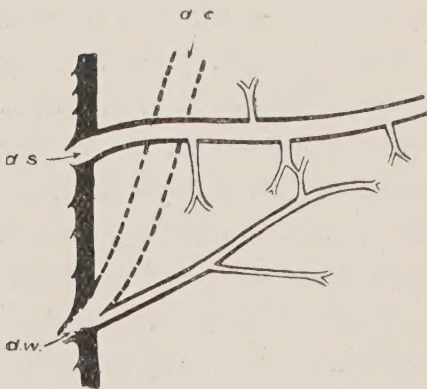


Fig. III.—Diagram after Opie. *d.s.*, Duct of Santorini; *d.w.*, duct of Wirsung; *d.c.*, ductus choledochus.

no communication between the two ducts would be possible. This leaves 30 per cent. of cases, and from these must be deducted 10 per cent. in which the duct of Santorini is the larger (Fig. III), and opens at the lesser papilla independently of the bile duct.

The experiments of Nordmann having demonstrated that bacteria can wander from the common bile duct into the duct of Wirsung through their contiguous walls, the complete blocking of the diverticulum



by a calculus would be pathologically effective to produce the disease without regurgitation of bile. Acute pancreatitis may presumably follow if the calculus remains sufficiently long in the diverticulum to cause stasis and infection of the pancreatic juice. This appears to have occurred in some cases of pancreatitis where a small stone has been found *post mortem* in the duodenum close to the papilla (Opie, also Balch and Smith).

In this connexion the frequency with which small stones are found in the gall bladder is significant, as shown in the London Hospital autopsies. The clinical histories of such cases tell of repeated attacks of biliary colic of short duration, coincident with the passage of small calculi down the common duct. Even when the diverticulum is absent and the two ducts open by separate orifices upon the summit of the bile papilla (Fig. IV)

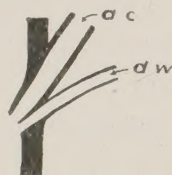


Fig. IV.—Diagram after Opie. Ductus choledochus and duct of Wirsung open by separate orifices.

a calculus impacted in the termination of the common bile duct might also occlude the pancreatic duct, as indicated in Fig. V. For example, in New's case (quoted by Egdahl) gall stones were present, but the duct of Wirsung had a separate opening.

It has been suggested that the passage of a stone may cause obstruction at the papilla from congestion. It is also probable that such a swelling and congestion may arise from a cholangitis, due to the passage of infected bile. In this way a cholecystitis without cholelithiasis may bring about acute pancreatitis; and it is quite clear that chronic pancreatitis, the causes of which are allied to those of the acute variety, is frequently due to cholecystitis without calculi. Balch and Smith<sup>10</sup>

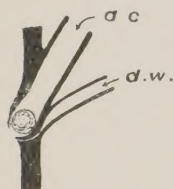


Fig. V.—Diagram to show how a calculus lodged at the orifice of the ductus choledochus may obstruct the duct of Wirsung when the two ducts open by separate orifices.

record a case of acute pancreatitis in which the ampulla was plugged with inspissated mucus.

Egdahl believes that, next to cholelithiasis, gastrointestinal diseases are the most common cause of acute

pancreatitis. He thinks that retrojection of bile may be caused by intestinal disorders closing the papilla. As we have already seen, the retrojection of bile is not essential provided there is closure of the papilla with infection of the bile.

An ascending infection of the biliary ducts would be likely to occur in gastro-duodenitis; 30 per cent. of Egdahl's cases belonged to this group, and 17 out of 32 gave a history of alcoholism. Three of his cases were associated respectively with duodenal perforation, gastric ulcer, and poisoning by oxalic acid. In two of the eleven London Hospital autopsies a duodenal ulcer was present.

Acute pancreatitis may occasionally be due to regurgitation of duodenal secretion. This is more likely to occur through the orifice of the duct of Santorini, which is not provided with a sphincter. Opie quotes (p. 153) a striking case of a man in whom pancreatitis was preceded by alcoholic gastritis and vomiting. The duct of Santorini was the principal outlet of the gland, as in Fig. III. Almost the entire gland was the seat of haemorrhagic inflammation, and the part about the small duct of Wirsung was apparently the least changed part of the organ. The orifice of the duct of Santorini readily admitted a probe about 2 mm. in diameter. In another case (Bassett's) the lesion was limited to a small area in the head of the gland, drained by a small duct of Santorini.

In two of Egdahl's cases acute pancreatitis was associated with enteric fever and in fourteen with mumps. The tendency of the typhoid bacillus to infect the biliary tract probably explains the association of acute pancreatitis with this disease. I operated successfully on a case of abscess of the head of the pancreas during convalescence from enteric fever.

#### *Sex and Age.*

A collection of 295 cases from literature shows that 63 per cent. of the cases are males and 37 per cent. females; the males therefore outnumber the females by nearly one-third. Deaver states that the number of males is twice as great as the females, but this is evidently an over-



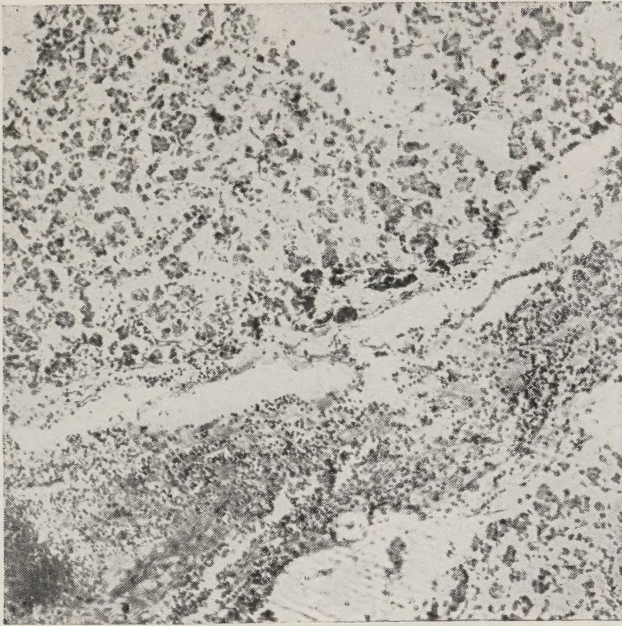


Fig. 1.—Microphotograph showing, above, necrosis of the parenchyma with red corpuscles diffused through the lobule. Below, a septum which is the seat of haemorrhage and necrosis. From a female, aged 62, who died on the sixth day of acute haemorrhagic pancreatitis.

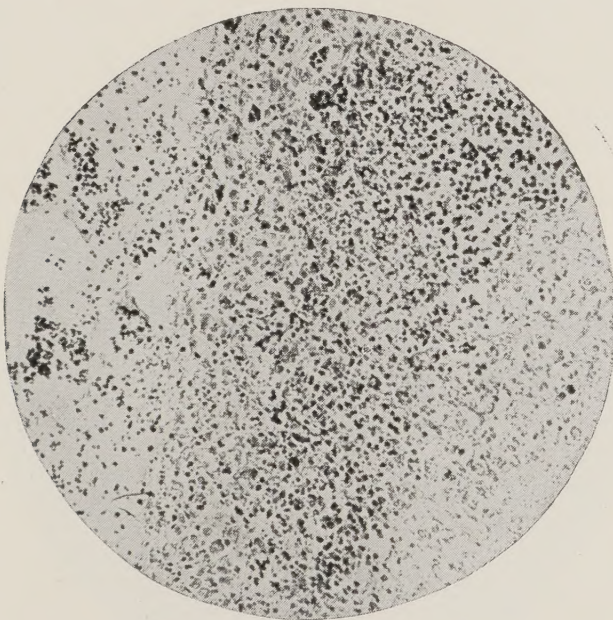


Fig. 2 shows, down the centre of the field, a dense infiltration of leucocytes at the margin of an area of necrotic parenchyma seen below and to the right of the field. To the left is a small group of red corpuscles. From a female, aged 30, who died on the second day with a round worm blocking the ducts of Wirsung and Santorini.



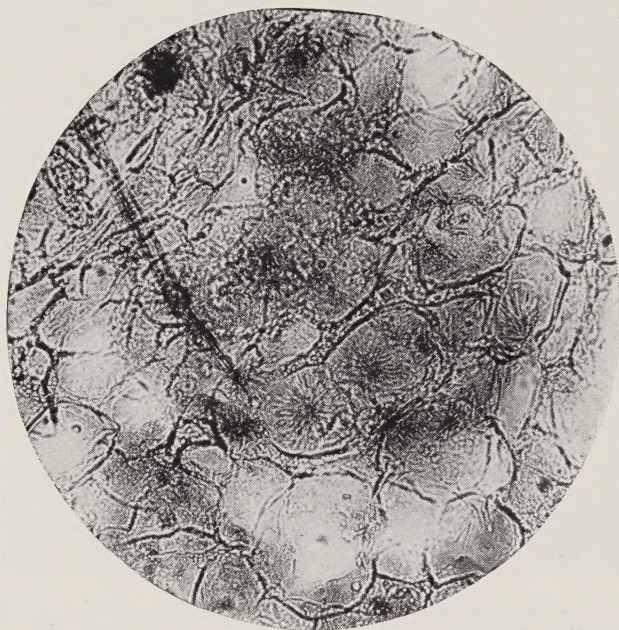


Fig. 3.—Slide showing fat necrosis. Crystals of oleic acid in the fat lobules are shown. Stained with Weigert's glia-mordant Sudan III and haematoxylin.

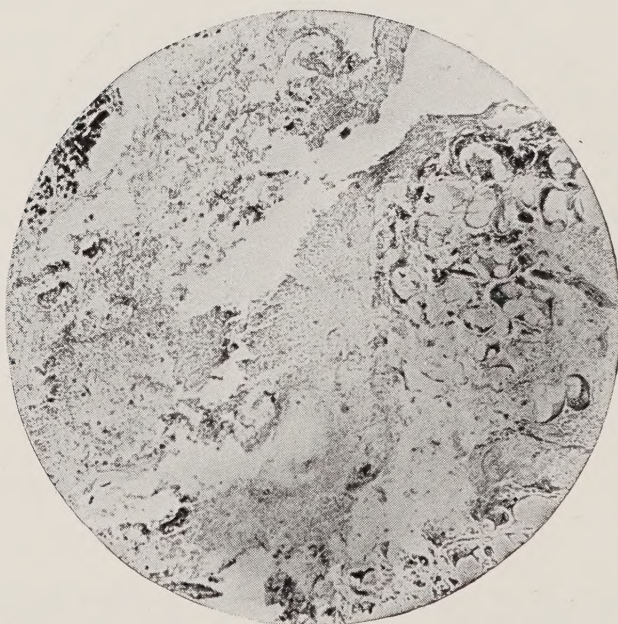


Fig. 4.—Slide showing to the right an area of fat necrosis; in the centre is necrotic connective tissue



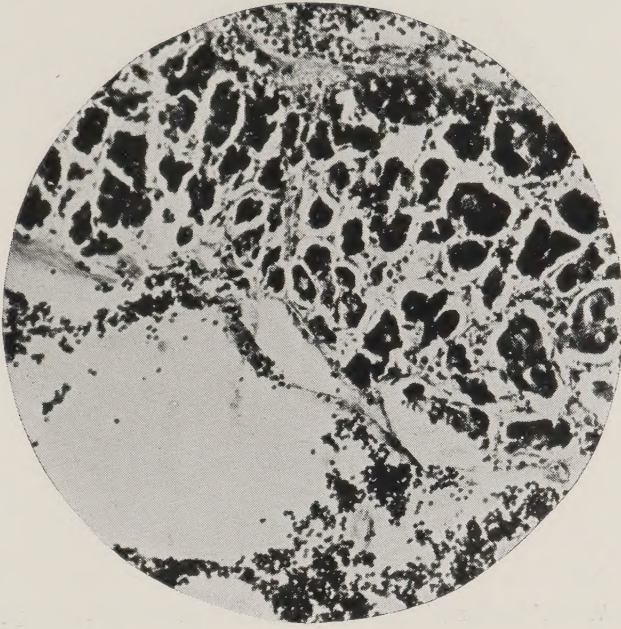


Fig. 5.—Slide showing haemorrhage, partial digestion of parenchyma and inter-acinar fibrosis. From a case of gall stones in the common duct.

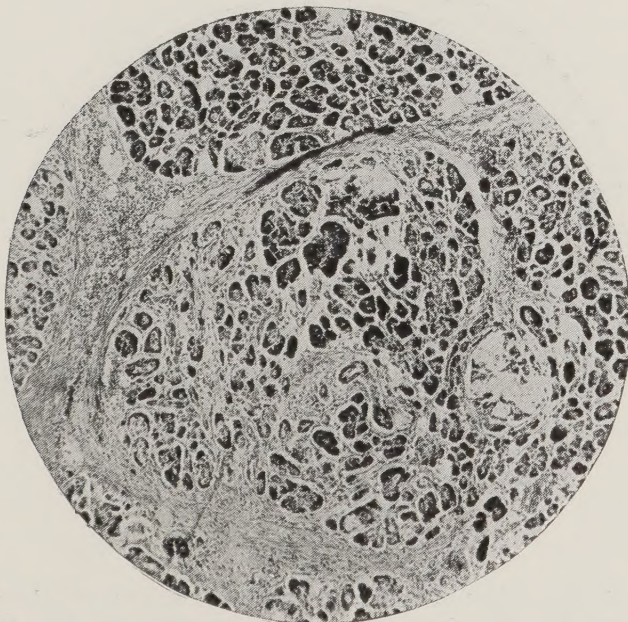


Fig. 6.—Slide from the same case, showing marked inter-lobular and inter-acinar fibrosis.



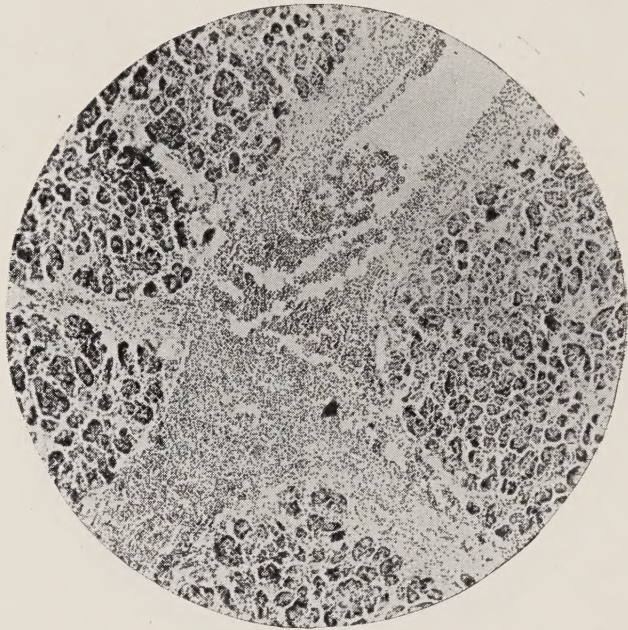


Fig. 7.—Slide showing purulent infiltration of the septa.

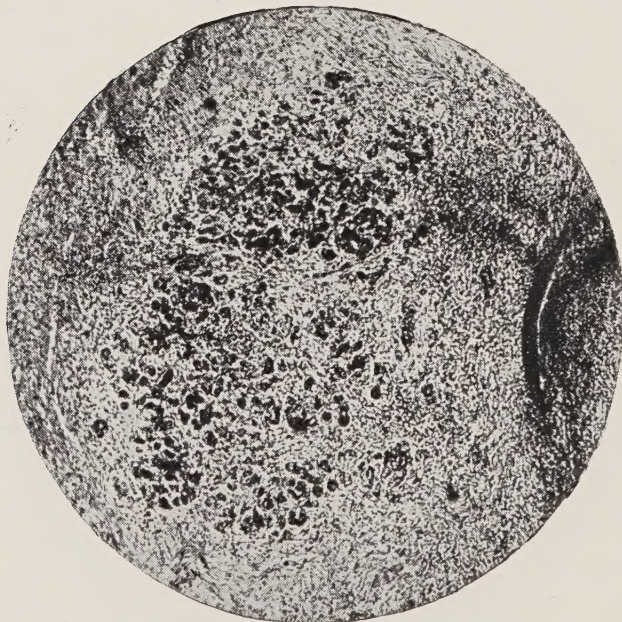


Fig. 8.—Slide showing extreme inter-lobular and inter-acinar fibrosis of the tail of the pancreas from the same patient, who died with diabetes. The dark patches towards the centre of the field are remains of acini separated by fibrous tissue.



estimate. The point is of importance, as it involves the relation of cholelithiasis to acute pancreatitis, the former being much commoner in women. The preponderance of males in acute pancreatitis is probably due to the fact that gastro-duodenal catarrh—especially the alcoholic form—and duodenal ulcer are more frequent among them.

The larger number of cases occur between the ages of 45 and 65. The addition of Dietrich's cases to those of the London Hospital shows that over 53 per cent. occurred during this period. In Körte's cases the greater number had reached the fourth or fifth decade. As an unusual circumstance it may be mentioned that 8 (30 per cent.) of the London Hospital patients were in the third decade.

#### CHRONIC PANCREATITIS.

Although we are mainly concerned with the subject of acute pancreatitis, it will not be out of place if we discuss briefly the pathology and etiology of chronic pancreatitis in the light of our review of the pathology of the former.

The relation of these two affections is far closer than would appear at first sight from a study of their morbid anatomy. Both are mainly the result of infection of the biliary and pancreatic ducts. Although they usually originate independently, yet a subacute pancreatitis may prove the starting-point of the chronic variety; and, on the contrary, the acute may be engrafted on a gland long affected with sclerotic changes. Two microscopic specimens from the Pathological Institute of the London Hospital illustrate the close relation as regards causation between acute and chronic pancreatitis. The first demonstrates an acute pancreatitis supervening on a chronic. The patient, a woman aged 49, had suffered for six months from biliary colic, and was jaundiced after the last attack. At an operation two large stones were found in the cystic duct, some smaller ones in the gall bladder, and some gritty matter in the common bile duct was pushed down by a probe which freely entered the duodenum. The gall bladder was much thickened and was removed; the dilated common duct was drained. The patient became weaker, jaundice appeared with vomiting, and she died on the twelfth day after the operation. At

the autopsy two calculi, which had probably receded during the operation into the hepatic duct, were found in the common bile duct, and there were acute haemorrhagic inflammation and fatty infiltration of the pancreas. On microscopic examination the ducts showed marked mucous catarrh. In parts were extensive haemorrhages with destruction of the parenchyma from digestion—in fact, acute haemorrhagic pancreatitis (Plate, Fig. 5). In addition there was considerable interlobular and inter-acinar fibrosis (Plate, Fig. 6) with infiltration of the fibrous tissue with lymphocytes, neutrophile leucocytes and some eosinophile leucocytes.

In this case the occurrence of jaundice after the operation suggests that obstruction of the common bile duct took place with acute infection of a pancreas already damaged by chronic infection due to calculi in the common bile duct.

The following case demonstrates an acute purulent inflammation of the ducts of the pancreas associated with extreme fibrosis of its tail.

The patient, a man aged 30, died with diabetes after exhibiting symptoms of it for three months. Fig. 7 (Plate), from the head of the gland, shows a portion of a septum which is thickly infiltrated with leucocytes. Fig. 8 (Plate), from the tail, exhibits extreme fibrosis both inter-lobular and inter-acinar. The inference drawn from this case is that a chronic infective catarrh of the pancreatic ducts had given rise to fibrosis and ultimately culminated in an acute suppurative inflammation.

The work of numerous experimenters proves that an acute pancreatic lesion which does not end fatally may terminate in chronic pancreatitis or in sclerosis. To quote only one set of experiments, Whipple, Chaffee, and Fisher<sup>11</sup> found that the injection of 3 to 5 c.cm. of bile into the pancreatic duct produced primarily an acute haemorrhagic lesion, and, secondarily, a chronic fibrous pancreatitis resulting from the healing of the acute inflammatory process. The pathological changes were controlled by exploratory laparotomies made respectively three and five weeks after the injection, at each of which a portion of pancreas was removed for microscopic examination; and some time subsequently an autopsy was made.



Nordmann, whose experiments have already been detailed, thought that in certain circumstances an inflammatory oedema was produced, which cleared up with complete recovery, but when cell infiltration was abundant the inflammatory changes gave rise to sclerosis—in other words, to chronic pancreatitis. I have observed clinically such a clearing up of an inflammatory oedema of the head of the pancreas. In the course of an operation for removal of a calculus from the common bile duct in a woman of 72, I found the head of the pancreas greatly swollen and softer than usual. A drainage tube was placed in the common bile duct. The patient died two weeks later of purulent bronchiectasis and pneumonia. Dr. Bartlett, who made a special examination of the pancreas for me, could find no microscopic change in the head of the gland. The gall bladder and ducts contained muco-pus, and bile obtained at the operation gave cultures of colon bacilli.

#### *Etiology.*

Like acute pancreatitis, the chronic form is closely related to cholelithiasis, especially to stones in the common duct, which would cause intermittent stasis of biliary and pancreatic secretion, and be associated with biliary infection. The often-quoted figures of the Mayos give 2,611 operations on the gall bladder and bile tract, with involvement of the pancreas in 200 cases (7.6 per cent.), and in 325 operations on the common and hepatic ducts the pancreas was affected in 22 per cent. Mayo Robson estimated that chronic pancreatitis existed in 60 per cent. of cases of calculi in the common bile duct.

Apart from the cases of chronic pancreatitis associated with cirrhosis of the liver, which I do not feel competent to discuss, a considerable number are unaccompanied by gall-stone disease. In many of these, however, cholecystitis exists, for in 73 cases of chronic pancreatitis in Deaver's<sup>12</sup> practice cholelithiasis existed in 35, and in 38 no calculi were present at the time of the operation. But of the non-calculus group 12 had demonstrable changes in the gall bladder, or, in other words, cholecystitis was present. The results of the operation of draining the gall bladder for chronic pancreatitis show that in a definite

proportion of cases the operation fails on account of a chronic form of cholecystitis which is not cured by drainage alone, although complete relief is obtained by cholecystenterostomy (W. J. Mayo<sup>22</sup> and Guerry<sup>23</sup>).

Morbid conditions of the duodenum play as important a rôle in the causation of chronic pancreatitis as in the acute form, and it has already been pointed out that gastro-duodenitis and ulcers favour the occurrence of an ascending infection of the biliary ducts, and that intermittent stasis may result thereby from congestion at the papilla.

Cancer of the head of the pancreas is in rare instances a cause of chronic pancreatitis. This is more readily understood when it is stated that Turnbull's records at the London Hospital show that practically all cases of so-called carcinoma of the head of the pancreas originate in the biliary or pancreatic ducts, and therefore from an early stage must cause stasis of the secretions in these ducts.

Certain cases of chronic pancreatitis coincident with gastric and duodenal ulcers are evidently due to direct microbic infection, either by extension from the base of the ulcer when it is adherent to the pancreas, or perhaps in some instances by the lymphatics.

Cambridge<sup>13</sup> gives the following summary of the causes of chronic pancreatitis from his notes of 414 cases. Fifty-one per cent. were secondary to some morbid condition of the digestive tract; 37 per cent. were associated with diseases of the biliary apparatus, chiefly gall stones; 8 per cent. were due to deposits of malignant disease from a primary deposit in some other organ; and 4 per cent. were probably dependent upon disease of the circulatory system. The proportion of cases due to diseases of the biliary apparatus is probably too low. The experiences of surgeons would probably show a larger number of cases dependent on this cause, many examples of chronic pancreatitis being discovered at operations for the relief of obvious biliary disease.

#### SYMPTOMS OF ACUTE PANCREATITIS.

In order to avoid the not uncommon error of repeating stereotyped descriptions of other authors, I have carefully



analysed 24 consecutive cases at the London Hospital of which the notes were complete, together with the abstracts of 16 cases given as an appendix to Dietrich's paper, making a total of 40 cases.

### *Premonitory Symptoms.*

Over one-half had premonitory symptoms of varying intensity. These consisted of attacks of pain in the upper abdomen, or occasionally over the abdomen generally (16 per cent.). As regards the cause of these attacks of pain, the symptoms and other indications lead to the conclusion that some of them were due to attacks of subacute pancreatitis. For example, in one London Hospital case several white spots, the remains of old fat necrosis, were observed in the subperitoneal fat at an operation for acute pancreatitis. This patient had suffered with attacks of pain for three years prior to the operation.

Körte observed fat necrosis, although its significance was not recognized, in a patient operated on for gall stones in 1895. At a second operation in 1896 for a stone in the common duct no signs of the former pancreatitis existed. Further, Körte saw four cases and Brentano three which were considered as examples of healed pancreatitis. The disappearance of fat necrosis in a short period has frequently been noted in experiments on animals. Polya observed after the injection of active trypsin into the pancreatic duct that, in those animals in which a relaparotomy was done for inspection, the areas of fat necrosis had disappeared between the laparotomy and their death. An animal which exhibited after laparotomy typical evidences of haemorrhage and fat necrosis showed on *post-mortem* examination, twenty - two days later, that all these changes had disappeared. In animals which lived for a week after the experiment fat necrosis was never found.

The premonitory attacks of pain were in a like proportion of cases (16 per cent.) referred to the right side of the upper abdomen. In many instances the pain resembled and might be referred to cholelithiasis, and in a few to duodenal ulcer. But a fair proportion of patients shown

subsequently to have gall stone disease complained of no previous symptoms.

A few cases gave a history of indigestion and flatulence.

### *Symptoms.*

These accord with the symptoms of the group of acute abdominal crises, and closely resemble those of perforation of gastric and duodenal ulcer, of the gall bladder, or the appendix. Many cases have been mistaken for acute intestinal obstruction. The onset is sudden, with very severe pain in the epigastrium, persistent vomiting, usually constipation, tenderness, fullness and resistance in the upper abdomen, and gradually increasing distension; the pulse is rapid and weak; the temperature lower than the pulse-rate, and not infrequently subnormal with collapse.

Körte, whose experience is probably unrivalled, says that the one symptom which gives the most probable insight into the condition is tenderness across the epigastrium, and resistance over the pancreas. He adds that the most distinctive sign is epigastric peritonitis, with subsequent swelling in the left lumbar region. This was present in 18 of his cases in which a diagnosis was possible.

There being no pathognomonic sign the diagnosis is admittedly difficult and uncertain, yet Dietrich states that in 16 cases admitted during the last five years to the Hamburg-Eppendorf Hospital, the nature of the malady was detected in the last 10. Obviously the difficulty must be greatest in very acute or in advanced cases, for in these there will be general abdominal tenderness and distension—in fact, the signs of general peritonitis. An analysis of the 40 cases mentioned above will indicate the frequency of the prominent symptoms.

Vomiting was almost a constant symptom (80 per cent.), and was often severe and incessant.

Constipation existed in 25 per cent., and was only marked in five cases. Diarrhoea was present in three cases, but in one of these the symptoms had existed fourteen days.

Pain was almost constant, and in 50 per cent. was situated in the epigastrium or upper abdomen. In the other cases it was localized in the right hypochondrium, the right side of abdomen, or right iliac fossa; in others on the left side or left iliac fossa.



Tenderness had much the same distribution as the pain. Distension existed in half the cases.

The most important fact resulting from this review of cases is that a swelling was only observed in 7 (17.5 per cent.)—twice in the right hypochondrium (in one of these being a distended gall bladder), thrice on the right side of the abdomen or to the right of the umbilicus, once on the left side of the abdomen, and once below the umbilicus. It may be observed that when pus forms around the pancreas it develops a retro-peritoneal collection and presents in the left flank, or passes through the gastro-hepatic omentum and forms a left-sided subphrenic abscess. Occasionally, as in a London Hospital case, it tracks retroperitoneally to the appendix region; a collection may also occur in the right kidney pouch, as it did in this case. Shivering was noted only twice. Jaundice was present in 5 cases (12.5 per cent.).

Cyanosis, sometimes spoken of as a characteristic sign, was only present twice; one was an acute case of twenty-four hours' duration, while in the other the symptoms had lasted fourteen days. Glycosuria was once noted, a trace of sugar being found in one of Dietrich's 16 cases. It existed in 8 of Korte's 44 cases. One patient of Korte developed diabetes one and a half years after extensive necrosis of the pancreas, and died eight years subsequent to the operations.

The discovery of fat necrosis during the operation is often the first definite indication of the nature of the malady. Its presence is very constant, but it was absent in 2 of Dietrich's 16 cases, one of these being a case operated on after forty-eight hours, and subsequently subjected to a *post-mortem* examination. The other, also an acute case of haemorrhagic pancreatitis, recovered after an operation, performed twenty-four hours after the onset.

Fat necrosis was stated to be absent in 4 of 27 consecutive London Hospital cases and all were subacute. This sign was therefore absent only in 14 per cent. of cases.

#### *Toxaemic Symptoms.*

The general condition of patients with acute pancreatitis is indicative of an acute toxaemia.

Speese, Sailer, and Torrey performed experiments on dogs<sup>14</sup> to ascertain if the toxaemia was due to the presence of trypsin in the blood serum. Pancreatitis was induced by injecting 20 c.c. of oil. As a result they concluded that there is no reason to believe that the toxaemia of acute pancreatitis is caused by any absorption of the external secretion of the pancreas. But they succeeded in

separating from the serum a substance lethal to guinea-pigs. They felt justified in saying that in acute pancreatitis the blood content in globulin is greatly increased and that either the globulin itself, or substances adherent to it, constitute the toxic element causing death in this disease.

#### *Cambridge's Reaction.*

Both clinicians and experimentalists have arrived at the conclusion that this reaction is of no definite value in the diagnosis of acute pancreatitis.

Körte found it negative in 7 out of 8 cases examined. Deaver, Ochsner, and Dietrich all state that it was of no assistance. Whipple, Chaffee, and Fisher<sup>15</sup> tested it in acute pancreatitis of dogs induced experimentally. They concluded that this test was of little value in establishing a diagnosis of acute pancreatitis in dogs. If the test is negative it is pretty strong evidence against an acute pancreatitis; but a positive Cambridge test is not infrequent in normal men and dogs. It is almost constantly present in chloroform poisoning in dogs, and may be present in cases of pneumonia, or in any condition where there are active cell destruction and autolysis. They add: "The method is open to various errors and too much depends on the personal equation, particularly in the interpretation of the various crystals."

#### TREATMENT.

There exists such a complete agreement as to the treatment of acute pancreatitis that this portion of the subject may be briefly dealt with.

Operation is indicated at the earliest moment that the disease is definitely suspected. Collapse should not be considered a legitimate cause of delay. Probably in the majority of cases this condition will only become deeper if operation be postponed; and our resources for combating shock have been considerably augmented during the last few years.

A median or right rectus incision is the direct channel for settling the diagnosis and exposing the pancreas. The biliary passages also require examination.

There are three routes by which the pancreas may be



exposed and the lesser cavity of the peritoneum opened up (see Fig. VI, after Mayo Robson).

1. Above the stomach, through the lesser or gastro-hepatic omentum. This can only be conveniently employed when gastropptosis exists.

2. Below the stomach through the upper part of the gastro-colic omentum. This is the method of choice.

3. Through the transverse meso-colon. This is inadvisable as haemorrhage may ensue, owing to wounding of large vessels (see Dietrich, Case VIII). The general peritoneal cavity is also less readily shut off.

4. In cases of localized abscess around or within the head of the pancreas, this may be exposed posteriorly by mobilizing the duodenum, or anteriorly by cutting through the peritoneum passing over the pancreas from the duodenum.

5. The tail of the pancreas may be reached by a transverse lumbar incision in the left costo-vertebral angle. This route should be adopted when the existence of a left lumbar swelling indicates the presence of a retroperitoneal collection of pus. After exposure of the gland through an anterior incision, it may also be used for the purpose of obtaining efficient drainage in cases of extensive necrosis, and it should never be omitted if there be a left lumbar swelling. In those cases where a left costo-vertebral incision is primarily employed for a swelling in the lumbar region, the anterior incision should not usually be dispensed with, for, as W. J. Mayo points out,<sup>16</sup> the head of the pancreas is most often involved. The justice of this advice appears evident from Körte's cases, which gave a mortality of 33 per cent. for those treated by abdominal incisions, and nearly 70 per cent. for cases in

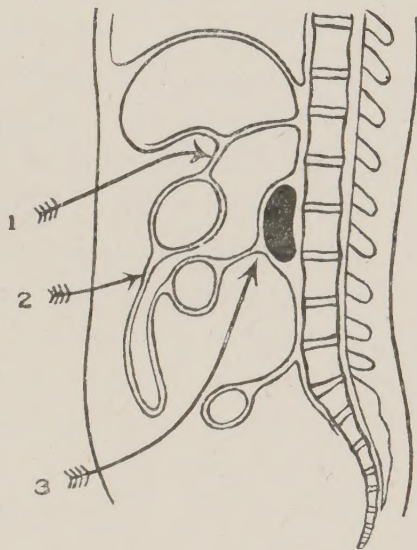


Fig. VI.—The peritoneal folds in relation to the pancreas. The arrows indicate three of the approaches to the gland. From *A System of Operative Surgery*, edited by F. F. Burghard.

which a lumbar incision was adopted. The latter, however, were often cases operated on in the later stages. They included also those operated on by the transpleural method.

6. Finally, a left subphrenic collection of pus should be opened either through an epigastric incision or by the transpleural route.

The procedure generally followed after opening the abdomen is to pack off the lower part of the peritoneal cavity with gauze, open the lesser cavity of the peritoneum through the gastro-colic omentum, and mop up any collection of sero-sanguineous or sero-purulent fluid within it. The covering of the pancreas is divided, and blunt scarification made along its whole length, or over the part affected, sometimes only the head. Bleeding is stopped by underrunning vessels with catgut, or a gauze plug is fixed in position with catgut sutures. A drainage tube is left in. If there is a quantity of fluid in the peritoneum a drain should be inserted above the pubes.

In those cases where a collection of pus exists, this should be drawn off by aspiration before the cavity is opened.

A careful examination of the biliary apparatus is an essential part of the operation. Cholecystotomy with drainage should be performed for calculi in the gall bladder or for cholecystitis; and choledochotomy with drainage should be carried out for calculi in the common duct, provided that the life of the patient is not imperilled by a prolongation of the operation. Cholecystectomy, if requisite, must be postponed till a later period.

#### RESULTS AND PROGNOSIS.

The mortality following operations for acute pancreatitis is still 40 to 60 per cent. But Ebner reports that of 20 cases not operated on only two recovered. In Dietrich's collection of 161 cases of various operators up to 1913, 98 died—a mortality of 61 per cent. These cases include 103 collected from literature by Körte in 1911. Körte's 34 personal cases in which the pancreas was exposed, gave a mortality of 47 per cent. (18 recovered and 16 died).



During the five years 1908 to 1912 inclusive, 17 cases were operated on at the London Hospital with 11 deaths, a mortality of 64.9 per cent.; while the series of 17 cases during the same period reported on by Dietrich gave a mortality of 77 per cent.

The prognosis depends mainly on the acuteness of the malady, and the period when operation is performed. Ultra-acute cases usually die with collapse in twenty-four to seventy-two hours; and extensive necrosis of the pancreas may be found as early as the third or fourth day.

Among the 6 London Hospital cases that recovered, 4 were definitely subacute, and one of them was not operated on till the fourteenth day of his illness; in this case and another there was no fat necrosis. But in the two remaining cases, operated on respectively on the second and fifth days, there was necrosis with sloughing.

Körte's cases give a valuable indication of the effect of their duration on the prognosis. The mortality in cases operated on in the first two weeks was 31 per cent.; of those operated on during the first three or four weeks 50 per cent.; of those operated on in the fifth and sixth weeks all died. In all cases operated on after the fourth week, necrosis of the pancreas and pus were found, and all died.

The prognosis in circumscribed abscess of the pancreas is favourable. Mayo Robson operated on 7 cases, with recovery in 6, though 2 of them succumbed later.

The patient may survive the operation and die subsequently from suppuration, chronic toxaemia, and exhaustion. One of my own patients died nine weeks after the operation, although a counter opening was made for drainage in the left loin, in addition to an anterior incision. At death very offensive pus and necrotic material were still discharging from the posterior opening. Fistulae exuding pancreatic secretion may remain for some time, but they usually close spontaneously. Another patient on whom I operated for pancreatitis occurring during convalescence from enteric fever still has a fistula some years after the operation. Haemorrhage is not an uncommon complication. It occurred in 7 of Körte's cases (20.6 per cent.) The haemorrhage always took place during the period of necrosis and pus formation, and was from the large arteries

along the upper border of the pancreas—four times from the splenic artery itself. All Körte's patients died except one, who was saved by plugging the wound with gauze.

#### TRAUMA.

The results of injury to the pancreas are of particular interest on account of their bearing on the nature of acute pancreatitis and pancreatic necrosis.

These injuries are usually produced by a blow on the epigastrium from a kick, or a blow from a buffer, shaft, etc.; or from a wheel passing over the abdomen. Some are the result of stabs or gunshot wounds. Not infrequently other abdominal organs are also implicated. The symptoms for the most part resemble those of acute or subacute pancreatitis.

A study of the clinical history of uncomplicated cases appears to me to justify their division into three groups:

1. Cases with fat necrosis and sero-sanguineous, or serous effusion into the lesser sac. These, as a rule, recover after laparotomy.
2. Cases with necrosis of the pancreas itself, haemorrhages, fat necrosis, and, in some instances, peritonitis. These are often fatal even after a timely laparotomy.
3. Cases of injury followed by the formation of a pseudocyst.

The pancreatic juice within the normal gland possesses no active proteolytic ferment, therefore injuries causing extravasation of the juice might be expected to produce only fat necrosis. This expectation is borne out by the cases in Group 1 and by experimental injuries. Opie found that fat necrosis followed division between two ligatures of the pancreatic ducts of cats. The pancreatic tissue was evidently opened up in separating the pancreas from the duodenum, otherwise there could have been no escape of juice, for it may be remembered that simple aseptic ligation of the ducts produces only fibrotic atrophy. The extent of the distribution of the fat necrosis was proportionate to the length of life of the animal. The peritoneal exudate was sterile. Opie also produced fat necrosis by transplanting the duodenal end of the pancreatic duct into the subcutaneous tissue of the abdomen.



As examples of Group 1 the following cases may be quoted :

The wheel of a cart passed over the abdomen of a boy aged 6. Laparotomy ten days after the injury showed abundant localized serous effusion and fat necrosis, with a visible lesion of the pancreas. The fluid was sterile. Recovery.<sup>17</sup> Hagedorn observed two similar cases operated on respectively twenty-four hours and seventeen days after the injury. Both recovered. In Hahn's case laparotomy revealed disseminated fat necrosis six months after a fall from a wagon. Recovery followed.

In Group 2 necrosis of the pancreas results either from destruction of its vitality or from interference with the circulation, owing to the severity of the injury; or, again as the result of primary or secondary infection of the injured tissue.

Selberg,<sup>18</sup> in a patient who died on the twentieth day after the kick of a horse, found microscopic evidence of necrosis of the entire pancreas.

In Opie's case of stab wound the patient died of streptococcic peritonitis, owing to a penetrating wound of the stomach, which was closed by operation. Around a puncture only of the pancreas there were found a haemorrhagic area with hyaline necrosis of the parenchyma and foci of fat necrosis, apparently due to the septic wound of the pancreas.

Levin,<sup>19</sup> as the result of numerous experiments, found that crushing of a part of the pancreas with artery forceps, or section of the gland at its middle between double ligatures, produced no effect. But if the vitality of the gland was seriously interfered with as by crushing and subsequent ligature of the main vessels, or by the application of six or seven ligatures around it, the animals died with "acute pancreatitis," and sometimes fat necrosis. Levin remarks that "peritoneal infection, which frequently occurs in these experiments, may be due to extraneous infection or to infection from the duodenum through the pancreatic duct."

On analysing Levin's experiments I find that nearly 50 per cent. of these very severe lesions of the pancreas were not fatal, and the autopsies showed only interstitial pancreatitis. Another element—almost certainly primary or secondary infection—must therefore have come into play, and determined the fatal issue in the remaining cases. This appears the more likely in view of our present knowledge that bacteria are capable of activating the pancreatic juice.

#### *Treatment.*

Exigencies of space permit me only to deal very briefly with this portion of my subject. The indication for operation

is quite as definite in the case of serious injuries of the pancreas, whether from subcutaneous trauma or gunshot and stab wounds, as in acute pancreatitis. The diagnosis must necessarily be uncertain, especially as other organs may be injured. But this is of little importance, in consideration of the fact that in most severe abdominal lesions laparotomy will be indicated. Von Mikulicz, in an admirable article on this subject,<sup>20</sup> specifies increasing anaemia, the physical signs of blood in the peritoneum, peritoneal irritation, and especially a steady accentuation of symptoms, as the indications of a severe injury to the pancreas.

After opening the abdomen haemorrhage from the pancreas must be stopped by deep sutures or by the use of the tampon, the injured area being packed off with gauze and drained. A break in the continuity of the organ may permit of a closure with deep sutures. A careful search for wounds of other viscera is necessary in all cases. The peritoneal cavity should be washed out with normal salt solution, for in the majority of cases pancreatic secretion will have escaped into it. The pancreatic juice, even when aseptic, is said to be highly toxic and to lower the resistance of the peritoneum to micro-organisms.

Von Mikulicz collected 45 cases of pancreatic injury; 21 were penetrating wounds, and 24 subcutaneous wounds from blunt force. Of the penetrating variety, 12 were gunshot and 9 stab wounds. Five of the gunshot wounds were operated on, with 2 deaths. The 7 that were not operated on died. The 9 stab wounds were all operated on, with only 1 fatality. These favourable results were due to the fact that the pancreatic injury was really a prolapse in 7 cases; and in some of these only a minor lesion of the prolapsed portion was present. Of the 24 subcutaneous injuries, 13 were not operated upon, and all died. Eleven were submitted to operation, and 7 recovered. The operations consisted in exposing the injured pancreas and in drainage.

In conclusion, I desire to express my indebtedness to Dr. Turnbull for much assistance and for generously placing the admirable records and the microscopic specimens of the Pathological Institute of the London Hospital



at my disposal; my sincere thanks are also due to Professor Starling and Dr. H. M. Vernon for valuable information, and to Mr. E. C. Lindsay for making abstracts of hospital notes and records.

## REFERENCES.

- <sup>1</sup> *Diseases of the Pancreas*, p. 159. <sup>2</sup> *Op. cit.*, p. 160. <sup>3</sup> *Johns Hopkins Hosp. Bull.*, 1911, p. 39. <sup>4</sup> *Journ. of Physiology*, vol. xlvii, p. 357. <sup>5</sup> *Mitteilungen aus den Grenzgebieten der Med. u. Chir.*, V, 24, 1912, p. 1. <sup>6</sup> *Arch. f. klin. Chir.*, V, 102, 1913, p. 66. <sup>7</sup> *Johns Hopkins Hosp. Bull.*, vol. xviii, p. 130. <sup>8</sup> *New York Med. Journ.*, vol. xcv, 1912, p. 572. <sup>9</sup> *Beiträge klin. Chir.*, Bd. 92, p. 322. <sup>10</sup> *Boston Med. and Surg. Journ.*, 1910, ii, p. 384. <sup>11</sup> *Johns Hopkins Hosp. Bull.*, vol. xxi, p. 339. <sup>12</sup> *Transactions*, College of Physicians, Philadelphia, vol. xxxiii, p. 83. <sup>13</sup> *Lancet*, 1911, i, p. 1494. <sup>14</sup> *Transactions*, Association of American Physicians, vol. xxvi, p. 446. <sup>15</sup> *Johns Hopkins Hosp. Bull.*, vol. xxi, 1910, p. 339. <sup>16</sup> *Surgery, Gynaecology, and Obstetrics*, vol. vii, 1908, p. 608. <sup>17</sup> *Dietrich*, *op. cit.* <sup>18</sup> *Berliner med. Woch.*, V, 38, p. 923. <sup>19</sup> *Journ. Med. Research*, vol. xvi, 1907, p. 419. <sup>20</sup> *Annals of Surgery*, vol. xxxviii, 1903. <sup>21</sup> *The Pancreas: Its Surgery and Pathology*, 1907. <sup>22</sup> *Amer. Journ. Med. Sci.*, April, 1914. <sup>23</sup> *Journ. Amer. Med. Assoc.*, December, 1910.

















